

PATENT SPECIFICATION

1,039,020

1,039,020



Inventor: JOHN CAMERON TURNER.

Date of filing Complete Specification: July 26, 1965.

Application Date: September 21, 1964.

No. 38403/64

Complete Specification Published: August 17, 1966.

© Crown Copyright 1966.

Index at Acceptance:—C2 C (2B24, 2B29).

Int. Cl.:—C 07 d 5/38.

COMPLETE SPECIFICATION

NO DRAWINGS

Process for the Preparation of 5-Nitrofurfuraldehyde Diacetate

We, BIOREX LABORATORIES LIMITED, a British Company, of 47-51, Exmouth Market, Rosebery Avenue, London, E.C.1., do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention is concerned with a new process for the preparation of 5-nitrofurfuraldehyde diacetate.

Numerous processes are known for the production of 5-nitrofurfuraldehyde diacetate. Thus, for example, this compound can be produced by first preparing a nitrating mixture from fuming nitric acid and acetic anhydride at 0°C. and adding dropwise to this nitrating mixture, a solution of furfuraldehyde diacetate in acetic anhydride, the temperature not being allowed to rise above 5°C. (see J.A.C.S., 52, 2551/1930).

In British Specification No. 679,202, there is described and claimed a process of nitrating furan compounds by means of nitric acid having a specific gravity not less than 1.42 and acetic anhydride to produce a nitration intermediate product and by treating said nitration intermediate product with a base, in order to convert said intermediate product into the corresponding 5-nitrofuran compound, said process being characterised by the feature that the nitration mixture, without isolating the intermediate product, is diluted with water, preferably with 1 to 3 parts by volume of ice water, and is adjusted to a pH within the range of 1.79 to 4.66, preferably of about 3.7, by the addition of a base, advantageously of trisodium phosphate, and the temperature of the diluted mixture is maintained at 25 to 60°C., preferably at about 55°C., during the addition of the

base and until the conversion of the intermediate product into the corresponding 5-nitrofuran compound is completed, the nitration mixture being cooled before or during the addition of the water.

Furthermore, in British Patent Specification No. 765,898, there is described and claimed a process for the preparation of 5-nitro-2-furfuraldehyde diacetate, which comprises nitrating furfuraldehyde with concentrated nitric acid and in the presence of acetic anhydride and in the presence of a small proportion of an arsenic compound.

In addition, British Patent Specification No. 797,961 describes and claims a process for the manufacture of 5-nitrofuran derivatives, which comprises reacting a furan derivative having an unsubstituted 5-position with concentrated or fuming nitric acid, in the presence of acetic anhydride and in the presence of a nitration catalyst comprising an acid-reacting compound

containing the group —SO or —SO₂, in an amount not exceeding 3% by weight of the acetic anhydride, and cooling the mixture during the nitration reaction.

All these previously known processes for the preparation of 5-nitrofurfuraldehyde diacetate suffer from a number of disadvantages. The fact that they all use concentrated or fuming nitric acid as the nitrating agent means that the nitration is rather difficult to control, must be carried out at low temperatures and also leads to the formation of undesired by-products, presumably due to the concurrent oxidising action of the nitric acid. The formation of undesired by-products also complicates the working up of the reaction mixture and the purification of the desired compound.

[Price

BEST AVAILABLE COPY

We have now found that furfuraldehyde can be readily converted into 5-nitrofurfuraldehyde diacetate in good yields, while avoiding the disadvantages of the previously known processes, the desired compound being obtained directly in a substantially pure form.

Thus, according to the present invention, there is provided a process for the production of 5-nitrofurfuraldehyde diacetate, wherein furfuraldehyde is nitrated, in the presence of acetic anhydride, with phosphoric acid and an alkali metal nitrate, such as sodium nitrate.

In a preferred method of carrying out the process according to the present invention, approximately 100% phosphoric acid is mixed, with cooling, with acetic anhydride and to this mixture there is then added a mixture of furfuraldehyde, acetic anhydride and sodium nitrate, the latter preferably being in finely-divided form.

The nitration reaction usually requires a certain amount of cooling: the temperature of the reaction mixture is preferably kept within the range of 30-50°C.

The reaction mixture can be worked up, for example, by warming with an aqueous solution of an alkali metal hydroxide, such as sodium hydroxide, and subsequently cooling, whereupon the desired 5-nitrofurfuraldehyde diacetate separates out and can be filtered off. After washing with dilute acetic acid and water, this diacetate is obtained in good yields and in a substantially pure form.

5-nitrofurfuraldehyde diacetate is a valuable intermediate for the preparation of pharmaceuticals, such as N-(5-nitro-2-furfurylidene)-1-amino-hydantoin, which is also known as nitrofurantoin. A particularly elegant method of preparing nitrofurantoin is the reaction of 5-nitrofurfuraldehyde diacetate with the product obtained by the reaction of potassium cyanate with ethyl hydrazino-acetic acid ester hydrochloride, a process for the production of this latter compound being described and claimed in our British Patent Specification No. 952,400.

The following Example is given for the purpose of illustrating the present invention:—

Example.

10 cc. approximately 100% phosphoric acid were added, with cooling, to 50 cc. acetic anhydride, 9.6 g. furfuraldehyde in

30 cc. acetic anhydride and 12.5 g. finely-divided sodium nitrate were added portion-wise, with cooling, to the mixture obtained. The temperature was kept at $40 \pm 3^\circ\text{C}$. for at least one hour.

The reaction mixture was then cooled and about 120 cc. 20% by weight aqueous sodium hydroxide solution were added, with cooling. The mixture was heated to a temperature not exceeding 60°C . for one hour and then cooled, 5-nitrofurfuraldehyde diacetate thereby separating out. This diacetate was filtered off and washed first with acetic acid and then with water. 5.6 g. substantially pure 5-nitrofurfuraldehyde diacetate were obtained with a melting point of 92°C .

WHAT WE CLAIM IS:—

1. A process for the production of 5-nitrofurfuraldehyde diacetate, wherein furfuraldehyde is nitrated, in the presence of acetic anhydride, with phosphoric acid and an alkali metal nitrate.
2. A process according to claim 1, wherein the alkali metal nitrate used is sodium nitrate.
3. A process according to claim 1 or 2, wherein a mixture of furfuraldehyde, acetic anhydride and sodium nitrate is added to a mixture of acetic anhydride and approximately 100% phosphoric acid.
4. A process according to any of the preceding claims, wherein the nitration is carried out at a temperature of $30-50^\circ\text{C}$.
5. A process according to any of the preceding claims, wherein the reaction mixture is worked up by warming with an aqueous solution of an alkali metal hydroxide, cooling and filtering off the separated 5-nitrofurfuraldehyde diacetate.
6. A process according to claim 1, for the production of 5-nitrofurfuraldehyde diacetate, substantially as hereinbefore described and exemplified.
7. 5-nitrofurfuraldehyde diacetate, whenever produced by the process according to any of claims 1 to 6.
8. N-(5-nitro-2-furfurylidene)-1-amino-hydantoin, whenever prepared from 5-nitrofurfuraldehyde according to claim 7.

H. A. L. VENNOR,
Chartered Patent Agent,
1, Great James Street,
Bedford Row,
London, W.C.1.
Agent for the Applicants.